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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,466	02/27/2004	Ranganatha Raghavan	PC27960A	8557

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WARNER-LAMBERT COMPANY
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ANN ARBOR, MI 48105

EXAMINER

FEDOWITZ, MATTHEW L

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 11/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/789,466	Applicant(s) RAGHAVAN ET AL.	
	Examiner Matthew L. Fedowitz	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 2/27/2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) ____ is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-15 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>06/01/2004</u> . | 6) <input type="checkbox"/> Other: ____ |

Art Unit: 1623

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) that forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

- 1) Determining the scope and contents of the prior art.
- 2) Ascertaining the differences between the prior art and the claims at issue.
- 3) Resolving the level of ordinary skill in the pertinent art.
- 4) Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-15 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Kennedy (US 5,912,237), Feller *et al.* (US 4,816,446), Teng (US 4,510,135), Kennedy *et al.* (US 3,330,327), Frederiksen (US 5,626,904), Huang *et al.* (CN 1,219,058 a), Martin *et al.* (Physical Pharmacy, Fourth Edition. Lea & Febiger 1993) and R. Simon (Dryers) Ltd. website (www.simon-dryers.co.uk/drum/index.htm Copyright 1998-2003).

Claim 1 is directed to a method for processing a solution containing heparin in a solvent or mixture of solvents to obtain a dry solid form of heparin using a drum dryer at atmospheric pressure or under a vacuum and at a suitable drying temperature. Claim 2 further limits claim 1 and is directed defining the heparin as a free heparin; or a salt of heparin with an alkali metal, alkaline earth metal, ammonium, tertiary ammonium or quaternary ammonium or any organic

Art Unit: 1623

base; or a complex of heparin with an inorganic or organic ammonium, tertiary amine or quaternary ammonium salt. Claim 4 further limits claim 2 wherein the heparin is heparin sodium. Claim 3 limits claim 1 wherein the heparin is heparin sodium. Claim 5 further limits claim 1 by requiring the solvent of the heparin solution to be water or water with water miscible solvents, or alcohols. Claims 6 and 7 further limit claim 5 by requiring the organic solvent to be an alcohol/mixture of alcohols or acetone, respectively. Claims 8 and 9 further limit claim 1 to a drum dryer that is a double or a single drum dryer, respectively. Claims 10 and 11 further limit the drying temperature of claim 1 to be between 20-210 degrees centigrade or 130-170 degrees centigrade respectively. Claim 11 further limits claim 1 by requiring the pressure to be between 0.001 mmHg and atmospheric pressure. Claim 13 further limits claim 11 to the pressure being atmospheric pressure. Claims 14 and 15 further limit claim 1 by the dry solid form of heparin being produced in less than 1 minute or 30 seconds, respectively, from initial contact of the heparin solution with the drum.

Kennedy teaches a reduced heparin solution containing a solvent (see column 7 lines 45-65), wherein the heparin used is heparin sodium (see Table VIII) and the use of water and other organic solvents such as ethanol (see column 7 lines 45-57 and column 8 lines 44-50)

Kennedy does not teach the use of a drum dryer (single or double) at atmospheric pressure or under a vacuum or the temperature ranges for drying. Kennedy also does not teach the use of free heparin or the use of heparin salts, other than heparin sodium, or heparin complexes. Moreover, Kennedy does not teach the use of a mixture of alcohols or acetone as a solvent.

As relating to claim 1, the R. Simon (Dryers) Ltd. website teaches that one of the many applications for both single and double drum dryers is their use in drying starches, which are polysaccharides in a similar manner that heparin is a polysaccharide. The site also teaches that vacuum casings and thermal efficiency are vital to the nature of drum dryers.

As relating to claim 2, Feller *et al.* teach that alkali and alkaline earth metal salts can be made with natural heparin (see column 5 lines 19-68 and column 6 lines 1-5). Teng teaches a method of making quaternary ammonium salts from heparin sodium (see column 6 lines 32-41) and a method of making tertiary and quaternary ammonium complexes (see abstract).

As relating to claims 3 and 4, Kennedy teaches the use of heparin sodium in making a dried heparin product (see Table VIII). Teng also teaches the use of heparin sodium in making ammonium salts and complexes (see column 6 lines 42-68). And Feller *et al.* teach the use of heparin sodium salts in the preparation of heparin derivatives (see column 5 lines 51-56).

As relating to claim 6 and 7, Feller *et al.* teach that teach the use of alcohols and acetone as a solvents (see column 7 lines 2-7).

As relating to claim 8 and 9, the R. Simon (Dryers) Ltd. website teaches that double drum dryers and single drum dryers can be used to dry starches, which are polysaccharides in the same manner that heparin is a polysaccharide.

As relating to claims 10, 11 and 13, Kennedy *et al.* teach a method of drying aqueous solutions of heat sensitive compounds using drum dryers. Specifically, Kennedy *et al.* teach that a satisfactory drying temperature for drum drying operations should be carried out under atmospheric pressure between about 210-280 degrees Fahrenheit (equivalent to 99-138 degrees

Art Unit: 1623

centigrade) as well as at 325 degrees Fahrenheit (equivalent to 163 degrees centigrade) (see column 2 lines 30-65 and column 3 lines 70-72 and column 4 line 1 and lines 15-22)

As relating to claim 12, Martin *et al.* teach that, according to the Clausius-Clapeyron Equation, it is well known in the pharmaceutical arts that when pressure is lowered the temperature of vaporization is also lowered thereby aiding in drying temperature sensitive products.

As relating to claims 14 and 15, Frederiksen teaches that a product can be dried on drum drier during a period of 1 to 60 seconds.

Therefore, it would have been obvious to one having ordinary skill in this art at the time the invention was made to obtain a method to produce a solid form of heparin having the above-cited references before him. By considering all the prior art cited it would lead one skilled in the art to have a reasonable expectation of success in combining Kennedy with the R. Simon (Dryers) Ltd. website and Feller *et al.* to obtain the process steps of claims 1-4 and 6-7; Kennedy with the R. Simon (Dryers) Ltd. website to obtain the process steps of claims 5, 8-9; Kennedy with the R. Simon (Dryers) Ltd. website and Kennedy *et al.* to obtain the process steps of claims 10, 11 and 13; Kennedy with the R. Simon (Dryers) Ltd. website and Martin *et al.* to obtain the process steps of claim 12; Kennedy with the R. Simon (Dryers) Ltd. website and Frederiksen to obtain the process steps of claims 14 and 15, to practice the invention as claimed to obtain the expected result, a method to produce a solid form of heparin.

Huang *et al.* provides the motivation to modify processes to produce a solid form of heparin because it is a goal of heparin manufacturing to increase production efficiency and to lower production costs by creating a continuous method of manufacturing (see abstract).

Art Unit: 1623

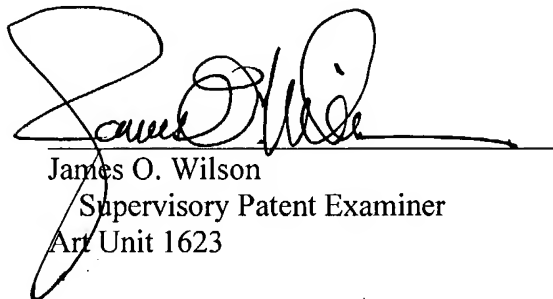
Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Matthew L. Fedowitz whose telephone number is (571) 272-3105. The examiner can normally be reached on 9am-5:30pm (EST) M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Matthew L. Fedowitz, Pharm.D., Esq.
November 12, 2004



James O. Wilson
Supervisory Patent Examiner
Art Unit 1623